REMARKS

Status of the Claims

Claims 12-22 and 27-30 are in the application.

Claims 12-22 and 27-30 were rejected.

Claims 12 and 30 have been amended and new claims 31 and 32 have been added.

Upon entry of this amendment, claims 12-22 and 27-32 will be pending.

Summary of the Amendment

Claim 12 has been amended. Claim 30 has been amended to correct a typographical error. Claims 31 and 32 have been added, support for which can be found throughout the application. No new matter has been added.

Claim Rejection Under 35 U.S.C. §112, second paragraph

Claims 12-22 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Office alleges that claim 12 is indefinite because the metes and bounds of the term "loop" cannot be determined from the language of the claim. The Office also alleges that claim 12 is indefinite because it is "unclear how the distal region can have 1-4 mismatches and have complete complementarity at its 5' end." (Office Action, page 3). Applicants respectfully disagree.

Claim 12 is definite because one of skill in the art could clearly understand the meaning of the terms and the metes and bounds of the claim. Applicants respectfully assert that claim 12 is definite, but solely to advance prosecution Applicants have amended claim 12 to further clarify the claim. Claim 12, step b, as amended states that the mRNA sequence

> b) includes a region corresponding to the loop region of the microRNA that either forms a loop of 2-5 non-paired nucleotides of mRNA when the loop region of the microRNA is 0, or <u>the mRNA</u> has 0 nucleotides when the loop region of the microRNA is

> 6-9 nucleotides, or the mRNA has 2-3 nucleotides which forms a bulge of 2-3 non-complementary nucleotides of mRNA when the loop region of the microRNA is 2-3 nucleotides

One of skill in the art would understand step b) of claim 12. The term "loop region" is defined in the specification. (see, Specification, ¶ 0023 of the published application). The specification states, that the "loop region of a microRNA"

> refers to the sequence of 0, 2-3 or 6-9 contiguous nucleotides starting at and including the nucleotide contiguous to the 3' end of the proximal region and ending at the nucleotide contiguous with the 5' end of the distal region

When the loop is zero (0) nucleotides, then the microRNA has no loop. The specification states, "when the loop region is 0 nucleotides, the 3' end of the proximal region is contiguous with … the nucleotide of the 5' end of the distal region." However, there is still a loop region of the microRNA, but it has zero nucleotides. The region is a descriptor of the sequence, but the region may not have any nucleotides in the sequence. This description of the loop region is set forth expressly in the claim. For example, claim 12 recites that

> when the loop region is 0 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the distal region, and when the loop region is 2-3 nucleotides or 6-9 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the loop region, and the 3' end of the loop region is contiguous to the 5' end of the distal region

Accordingly, one of skill in the art reading the claims with reference to the specification would be able to understand when and how the loop region is present in the microRNA or the mRNA.

The Office also alleges that step c) is unclear because it is "unclear how the distal region can have 1-4 mismatches and have complete complementarity at its 5' end." Applicants respectfully assert that the Office is misreading the claim. Claim 12, step c) recites that the mRNA

> includes a region corresponding to the distal region of the microRNA that is **either**: (i) completely complementary to at least 7 contiguous nucleotides of the distal region of the microRNA,

> including the 5' end of the distal region, **or** (ii) contains (A) mismatches of 1-4 contiguous nucleotides and (B) matches of at least 5 nucleotides to a contiguous nucleotide sequence of the distal region of the microRNA, including the 5' end of the distal region; (emphasis added)

Step c) does not state that the distal region can have 1-4 mismatches **and** have complete complementarity at its 5' end. Step c) uses the terms "either" and "or" in references to these structural features. Therefore, one of skill in the art reading step c) would understand that the distal region does not have both complete complementarity and 1-4 mismatches as the Office has alleged because of the use of the terms "either" and "or."

Accordingly, the claims are definite because one of skill in the art would understand the metes and bounds of the claims. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claim Rejections Under 35 U.S.C. § 101

Claims 12-22 and 27-30 stand rejected under 35 U.S.C. § 101 as allegedly encompassing non-statutory subject matter. The Office alleges that the processes are not tied to a particular machine or that the process does not transform an article to a different state or thing. Applicants respectfully disagree that the presently claimed invention is directed to non-statutory subject matter.

The presently claimed invention is patentable subject matter because it is not an abstract idea. In contrast to an abstract idea, the presently claimed methods are a practical application that can be used to generate microRNA, which are useful for regulating gene expression. The Office has used the incorrect standard to determine whether or not the presently claimed subject matter should be rejected under 35 U.S.C. § 101. The Office used the test set forth in *In re Bilski*, (545 F. 3d 943 Fed. Cir. 2008). Recently, the Supreme Court rejected the Federal Circuit test as too narrow and that "The machine-or-transformation test is not the sole test for deciding whether an invention is a patent-eligible 'process.'" (*Bilski v. Kappos*, 130 S. Ct. 3218, 3227,

2010). Under the standard set forth in the Supreme Court's *Bilski* decision, the presently claimed invention is patentable under 35 U.S.C. § 101.

The presently claimed invention is directed to a method of generating a microRNA. The method describes concrete steps to identify and generate the microRNA, which is a practical application and not an abstract idea. The generation of a microRNA is not abstract. The presently claimed invention is not directed to an abstract idea as was the invention in *Bilski*. The Office has not shown that the presently claimed invention is an abstract idea, and, therefore, the Office has not satisfied its burden to show that the presently claimed invention is unpatentable under 35 U.S.C. § 101.

Furthermore, even if the Federal Circuit Test were the proper test, the presently claimed invention is still patentable under 35 U.S.C. § 101. The claim recites a step of "generating an oligonucleotide sequence that is 17-25 nucleotides and has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA-recognition element for a microRNA." This step creates a microRNA, which is a product even if the microRNA is not physically made. The generation of a product even if not physically synthesized is not abstract. Furthermore, claims 18-22 and 27-30 either specifically synthesize the microRNA, use a synthesized microRNA, or the method/system is tied to a particular machine or apparatus. Therefore, all the claims satisfy the criteria of the Supreme Court and those set forth in the Federal Circuit decision. Accordingly, the claims are patentable under 35 U.S.C. § 101.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

Claim Rejections Under 35 U.S.C. § 102

Claims 12-22 and 27-30 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Bentwich (US Application Publication No. 20060003322). The Office alleges Bentwich teaches each and every element of the claim. Applicants respectfully disagree.

Bentwich fails to anticipate the presently claimed invention because Bentwich fails to disclose each and every element of the presently claimed methods as they are arranged in the presently pending claims. For a reference to anticipate a claim, the reference must disclose either explicitly or inherently each and every element of the claim. Additionally, for a reference to anticipate a claim the reference "must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements 'arranged as in the claim.'" *NetMoney v. Verisign* 545 F.3d 1359, 1369 (Fed. Cir. 2008). Bentwich fails to anticipate the claim because the reference fails to disclose each and every element as they are arranged in the presently claimed invention.

Bentwich fails to disclose a method of identifying a selected mRNA sequence to be the target of the microRNA and generating a microRNA based upon the steps in the claims. The presently claimed invention is directed to a method of generating a microRNA by identifying the target and then generating a microRNA. The claims recites specific steps that are used to generate a microRNA. These steps are recited in claim 12. The complementarity of the microRNA to the target mRNA are recited in steps a) through c). The Bentwich fails to recite any of these steps as they are recited in the claims. The Office makes a generalized conclusion that "Bentwich teaches a system for identifying and generating microRNA" comprising the characteristics described in the presently claimed invention (see, Office Action, pp. 4-5). The Office refers Applicants to the abstract, pages 1-2, and figures 8-10, 16, 21, 22, and 24-26 of Bentwich. The abstract of Bentwich states:

> The present invention relates to a first group of novel genes, here identified as "genomic address messenger" or "GAM" genes, and a second group of novel operon-like genes, here identified as "genomic record" or "GR" genes. GAM genes selectively inhibit translation of known `target` genes, many of which are known to be involved in various diseases. Nucleic acid molecules are provided respectively encoding 20600 GAM genes, and 6635 GR genes, as are vectors and probes both comprising the nucleic acid molecules, and methods and systems for detecting GAM and GR genes and specific functions and utilities thereof, for detecting

> expression of GAM and GR genes, and for selectively enhancing and selectively inhibiting translation of the respective target genes thereof.

Notably, the abstract does not describe a method of identifying a target and generating a microRNA. Rather the abstract refers to novel genes that have been identified and that nucleic acid molecules encoding the genes are provided. The abstract provides no details on how the genes were identified or how the nucleic acid molecules were generated.

Furthermore, Figures 8-10 fail to disclose or suggest the presently claimed methods. Figures 8-10 and 16 are flowcharts or diagrams that describes how to detect bioinformatically a group of novel genes or how the novel genes can be used to inhibit a target gene. The flowcharts and diagrams, however, do not describe a method of identifying a target and generating a microRNA as presently claimed. Figure 21 and 22 show an annotated sequence along with some laboratory results confirming expression of the novel gene. Figures 21 and 22, however, fail to disclose a method of generating microRNA as is presently claimed. Figures 24-26 illustrates a mechanism of inhibiting a target gene's expression and various nucleic acid sequences' complementarity to other sequences. Figures 24-26, however, fail to disclose a method of identifying a target and generating microRNA as is presently claimed. Applicants have been unable to identify anywhere in Bentwich that discloses or suggests the presently claimed method. Therefore, Bentwich fails to teach the presently claimed methods or systems implementing the methods.

The present rejection under 35 U.S.C. § 102 appears to rely on the fact that some of the examples shown in Figures 24-26 may have the same complementarity that are described in the presently claimed methods. Applicants, note, however, the presently claimed methods are not apparent based upon the product itself. A method is not anticipated by the product unless the product alone is able to describe the method. The Office has failed to show where the presently claimed methods are disclosed in Bentwich either explicitly or implicitly by the products.

Furthermore, Applicants were unable to identify a sequence in Bentwich, where the mRNA includes a region corresponding to the loop region of the microRNA that either forms a loop of 2-5 non-paired nucleotides of mRNA when the loop region of the microRNA is zero (claim 31) or the mRNA has 0 nucleotides when the loop region of the microRNA is 6-9 nucleotides (claim 32). Therefore, even if the method were anticipated based solely on the product, which it is not, claims 31 and 32 are not anticipated because Applicants were unable to identify examples that would anticipate claims 31 and 32. However, as discussed above, the method is not anticipated by the product. The presently claimed method is directed to the steps and characteristics cited in the claims not the microRNA that is generated by the method. These characteristics and steps are not described or even suggested in Bentwich. Bentwich describes a sequence that is a "partial inversed-reversed sequence." This "partial inversed-reversed sequence," however, fails to have the characteristics and steps recited in the presently claimed invention. Thus, Bentwich fails to anticipate the pending claims. If the Office maintains the rejection, Applicants respectfully request the Office to point out where the presently claimed methods are disclosed.

Therefore, in view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102 be withdrawn.

Conclusion

Claims 12-27 and 30-32 are in condition for allowance. A notice of allowance is earnestly solicited. Applicants invite the Examiner to contact the undersigned at 610.640.7820 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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